Hepatitis, D and E, Acute

(Previously Hepatitis, Unspecified)

1. DISEASE REPORTING

A. Purpose of Reporting and Surveillance

1. To better characterize the epidemiology of infectious hepatitis not due to hepatitis A, B, or C viruses.
2. To recommend appropriate preventive measures, including immunization against other types of hepatitis which are vaccine-preventable.

B. Legal Reporting Requirements

1. Health care providers: notifiable to local health jurisdiction within 3 work days
2. Hospitals: notifiable to local health jurisdiction within 3 work days
3. Laboratories: no requirements for reporting
4. Local health jurisdictions: notifiable to Washington State Department of Health (DOH) Communicable Disease Epidemiology Section (CDES) within 7 days of case investigation completion or summary information required within 21 days

C. Local Health Jurisdiction Investigation Responsibilities

1. Begin investigation within one working day.
2. Facilitate transport of specimens to Public Health Laboratories for confirmatory testing.
3. Initiate appropriate infection control measures.
4. Hepatitis D virus and hepatitis E virus infections should be reported to DOH as unspecified infectious hepatitis. Report all *confirmed* cases to CDES. Complete the hepatitis, unspecified report form (http://www.doh.wa.gov/notify/forms/hepu.pdf) and enter the data in the Public Health Issues Management System (PHIMS).

2A. HEPATITIS D AND ITS EPIDEMIOLOGY

Background

Hepatitis D infections occur globally, but the prevalence varies widely among countries. An estimated 10 million people worldwide have dual infections with hepatitis D and hepatitis B viruses. Hepatitis D infection occurs epidemically or endemically in populations at risk of hepatitis B virus infection, such as populations in countries where hepatitis B is endemic (e.g., Russia, Romania, southern Italy, Africa and South America); in hemophiliacs, intravenous drug addicts and others who come in frequent contact with blood; in institutions for the developmentally disabled; and, to a lesser extent, in male homosexuals.

A. Etiologic Agent

Hepatitis D virus is an "incomplete virus" because it can only replicate in the presence of Hepatitis B virus. Hepatitis D virus has a small single-stranded RNA genome that only encodes one virus-specific protein ("delta antigen"). This genome is encapsulated within a protein coat of HBsAg that allows the hepatitis D virus to gain cell entry. During the period when hepatitis D virus is replicating in cells, hepatitis B replication in temporarily suspended.

B. Description of Illness

Onset is usually abrupt, with signs and symptoms resembling those of infections with hepatitis B virus; illness may be severe. Hepatitis D virus transmission can occur simultaneously with a new hepatitis B infection ("co-infection") or can occur as a superinfection of a person with chronic hepatitis B. Hepatitis D may be self-limiting or it may progress to chronic hepatitis. Children may have a particularly severe clinical course with common progression to chronic active hepatitis. With superinfection, symptoms due to hepatitis D infection can be misdiagnosed as an exacerbation of chronic hepatitis B infection.

C. Hepatitis D in Washington State

An outbreak of acute hepatitis B infection among injecting drug users in Pierce County in April 2000 included 60 cases and also involved cases of hepatitis D infection. The three deaths in the outbreak were all infected with hepatitis B and D viruses.

D. Reservoirs

Humans.

E. Modes of Transmission

Transmission is similar to that of hepatitis B virus – by exposure to infected blood and serous body fluids, contaminated needles, syringes and plasma derivatives such as antihemophilic factor, and through sexual transmission. All people still susceptible to hepatitis B virus infection or who have chronic hepatitis B infection can be infected with hepatitis D virus.

F. Incubation Period

Approximately 2–8 weeks.

G. Period of Communicability

Blood is potentially infectious during all phases of active hepatitis D infection. Peak infectivity probably occurs just prior to onset of acute illness, when particles containing the hepatitis D antigen are readily detected in the blood. Following onset of symptoms, viremia probably falls rapidly to low or undetectable levels but experimental evidence suggests infectivity may persist even if antigen is not detectable.

H. Treatment

Treatment for acute hepatitis D infection is supportive. For chronic hepatitis B and D virus infection, antiviral treatment for hepatitis B or, in severe cases, liver transplantation may be considered.

2B. HEPATITIS E AND ITS EPIDEMIOLOGY

Background

After hepatitis A, hepatitis E virus is the second most common etiologic agent of enterically transmitted viral hepatitis throughout the world. Outbreaks and sporadic cases of hepatitis E infection occur over a wide geographic area especially in areas with inadequate environmental sanitation. Outbreaks are often waterborne, but sporadic cases and epidemics not clearly related to water have been reported; foodborne outbreaks have been reported. The highest rates of hepatitis E infection are in young to middle-aged adults although lower rates in younger age groups may reflect undiagnosed milder hepatitis E infections without jaundice. In the United States and most other industrialized countries, almost all cases result from travel to hepatitis E virus endemic areas.

A. Etiologic Agent

The hepatitis E virus (HEV) is a single-stranded RNA virus.

B. Description of Illness

The clinical course is usually like that of hepatitis A. The case-fatality rate is similar to that of hepatitis A except in pregnant women, where the rate may reach 20% for those infected during the third trimester of pregnancy. Severe cases of hepatitis E in Japan have been associated with a more virulent genotype of the virus (Emerg Infect Dis 2009 May). Chronic hepatitis E has been described in a small number of organ-transplant recipients in Europe (NEJM 2008;358(8):814) but chronic infections are very rare.

C. Hepatitis E in Washington State

Two cases have been reported in the past five years, both associated with travel to India.

D. Reservoirs

Humans. Wild and domestic animals, particularly swine.

E. Modes of Transmission

Hepatitis E virus is transmitted primarily by the fecal-oral route and fecally contaminated drinking water is the most commonly documented vehicle of transmission. Fecal-oral transmission probably can occur from person-to-person, though secondary household cases are not common during outbreaks. Recent studies have suggested that hepatitis E is likely a zoonotic infection transmitted from domestic pigs and other wild animal species.

F. Incubation Period

The range is 2 to 9 weeks; mean incubation period is around 6 weeks but has varied from 26 to 42 days in different epidemics.

G. Period of Communicability

Not known. However, hepatitis E virus has been detected in stools 14 days after the onset of jaundice and approximately 4 weeks after ingestion of contaminated food or water and persists for about 2 weeks.

H. Treatment

Treatment is supportive.

3. CASE DEFINITIONS

A. Clinical Description

An illness with a) discrete onset of symptoms **and** b) jaundice or elevated serum aminotransferase levels.

B. Laboratory Criteria for Diagnosis

Hepatitis D

- Serum aminotransferase levels > 2.5 times the upper limit of normal, **and**
- Immunoglobulin M (IgM) anti-HAV negative, **and**
- Anti-HCV negative, **and**
- HBsAg or IgM anti-HBc positive, **and**
- Positive result from a research laboratory for hepatitis D RNA or detection of antibody to hepatitis D virus.

Hepatitis E

- Serum aminotransferase levels > 2.5 times the upper limit of normal, **and**
- Immunoglobulin M (IgM) anti-HAV negative, **and**
- IgM anti-HBc negative (if done) or HbsAg negative, **and**
- Anti-HCV negative, **and**
- Positive result from a research laboratory for hepatitis E RNA or detection of antibody to hepatitis E antigen.

C. Case Definition (DOH)

Confirmed: A case that meets the clinical case definition and is laboratory confirmed.

4. DIAGNOSIS AND LABORATORY SERVICES

A. Diagnosis

Diagnosis of hepatitis D depends on clinical and epidemiologic features and exclusion of other etiologies of hepatitis, especially hepatitis A, by serologic means. EIA is available to detect total antibody to hepatitis D virus (anti-HDV). A positive IgM titer indicates ongoing replication; reverse transcription PCR is the most sensitive assay for detecting hepatitis D viremia.

Diagnosis of hepatitis E depends on clinical and epidemiologic features and exclusion of other etiologies of hepatitis, especially hepatitis A, by serologic means.

Several diagnostic tests are available including enzyme immunoassays and Western blot assays to detect IgM and IgG anti-HEV in serum; polymerase chain reaction tests to detect hepatitis E virus RNA in serum and stool; and immunofluorescent antibody blocking assays to detect antibody to hepatitis E antigen in serum and liver.

B. Tests Available at the Washington State Department of Health Public Health Laboratories (PHL)

PHL does not perform testing for hepatitis D or E but will forward specimens to the Centers for Disease Control and Prevention for testing or confirmation. Please contact Communicable Disease Epidemiology Section for approval prior to submitting specimens.

C. Specimen Collection

Serum should be refrigerated and transported cold. Specimens should be submitted with a completed DOH PHL Virus Examinations form available at: http://www.doh.wa.gov/EHSPHL/PHL/Forms/SerVirHIV.pdf

5. ROUTINE CASE INVESTIGATION

Interview the case or others who may be able to provide pertinent information.

A. Evaluate the Diagnosis

Confirm that the case's illness is consistent with acute viral hepatitis. Diagnosis is supported by presence of risk factors such as intravenous drug use for hepatitis D or international travel for hepatitis E. Facilitate transport of positive specimens to Public Health Laboratories for confirmatory testing.

B. Identify Potential Sources of Infection

Ask the case about potential exposures 2–8 weeks before onset of illness, including any persons (e.g., household member, sex partners, shared injection equipment, shared a meal, others in a travel group) who had a compatible illness. Obtain each person's name and contact information. Newly identified suspected cases should be reported and investigated in the same manner as the index case.

C. Identify Close Contacts or Others Potentially Exposed to the Patient

1. For hepatitis D investigations, identify secondary cases, that is, persons potentially exposed to the case during the communicable period. These include household members, sexual contacts, and needle sharing contacts and others potentially exposed to blood or sexual fluids. Evaluate for symptoms and educate about preventing transmission. Recommend hepatitis B vaccination to contacts susceptible to hepatitis B virus.
2. Secondary cases of hepatitis E infection are not common.
3. If the case has donated blood or plasma in the 8 weeks before onset, see Section 7C.
4. If the patient is pregnant, see Section 7D.

D. Environmental Evaluation

None, unless a commercial food service facility, child care center, or public water supply appears to be implicated as the source of infection.

6. CONTROLLING FURTHER SPREAD

A. Infection Control Recommendations / Case Management

1. Hepatitis D: Hospitalized patients should be cared for using standard precautions.

2. Hepatitis E: Hospitalized patients should be cared for using standard precautions. In addition, contact precautions should be used for diapered or incontinent individuals for the duration of symptoms.
3. Patients infected with hepatitis D or hepatitis E viruses who are still susceptible to hepatitis A should be vaccinated against hepatitis A.

B. Contact Management

1. Symptomatic Contacts

Symptomatic close contacts of a confirmed case should be referred to a healthcare provider and tested.

2. Postexposure Prophylaxis

No products are available to prevent hepatitis D or E in contacts.

3. Education

All persons exposed to the case or the same source as the case should be educated about signs and symptoms of hepatitis in both children and adults, and methods to prevent transmission. They should be informed that persons may be infectious without being ill.

4. Vaccination

For contacts of hepatitis D cases who are still susceptible to hepatitis B virus, recommend hepatitis B vaccination.

7. MANAGING SPECIAL SITUATIONS

A. Case is a Health Care Worker with Hepatitis D

If the case is a dentist, physician, nurse, or other health care worker with potential for exposing patients by blood or other body fluids:

1. Discourage the person from working until the acute clinical illness has resolved;
2. Recommend that upon return to work, the worker practice special precautions be practiced until no longer infectious, including:
   a. wearing gloves for all procedures during which the hands will be in contact with patients' mucosal surfaces or broken skin;
   b. avoiding situations involving sharps that could lead to exposures of susceptible patients to blood or objects contaminated with blood of the case;
   c. careful and frequent hand washing.
3. Chronically infected health care workers should be encouraged to voluntarily seek confidential counseling from employee health services regarding risk reduction strategies, which evaluation would include a review of their practice by an expert panel.

B. Outbreak of Hepatitis D

When two or more cases occur associated with a common exposure, such as a health care setting, conduct a search for additional cases. If a plasma derivative such as antihemophilic factor, fibrinogen, pooled plasma or thrombin is implicated, notify the

bloodbank to withdraw the lot from use and trace all recipients of the same lot.

Provide education and outreach to intravenous drug users in the community to reduce bloodborne transmission and make available hepatitis B vaccination for those still susceptible to that infection.

C. Outbreak of Hepatitis E

Follow investigation guidelines for foodborne or waterborne outbreaks.

See: Said B, Ijaz S, Kafatos G, Booth L, Thomas HL, et al. Hepatitis E outbreak on cruise ship. Emerg Infect Dis [serial on the Internet]. 2009 Nov [*cited 10/26/2009*]. http://www.cdc.gov/EID/content/15/11/1738.htm

D. Case Is a Recent Blood Donor or Recipient

The blood bank should be notified so that any unused product can be recalled.

E. Case Is Pregnant

Follow the perinatal hepatitis B recommendations if the pregnant woman is hepatitis B virus DNA or HBsAg-positive.

Hepatitis E virus infection can be severe in a pregnant woman, causing acute liver failure and premature delivery or stillbirth. Consult with Communicable Disease Epidemiology Section.

8. ROUTINE PREVENTION

A. Immunization Recommendations

None. Multiple viral hepatitis infections can result in liver damage, so universal immunization is recommended to prevent hepatitis A and hepatitis B.

B. Prevention Recommendations

1. Hepatitis D

Preventing hepatitis B virus infection prevents infection with hepatitis D virus. For at-risk persons such as injection drug users, follow prevention recommendations for hepatitis B including vaccination for those susceptible to hepatitis B virus infection. Among persons with chronic hepatitis B virus, the only effective measure is avoiding exposure to any potential source of hepatitis D. Immune globulin, hepatitis B immune globulin, and hepatitis B vaccine do not protect persons with chronic hepatitis B virus from infection by hepatitis D virus. Studies suggest that measures which decrease sexual exposure and needle sharing have been associated with a decline in the incidence of hepatitis D virus infection.

2. Hepatitis E

Routine precautions should be taken during travel in risk areas to assure safe food and water, particularly for women who may be pregnant. Hepatitis E is highly endemic in many parts of Asia and Africa, but is also endemic in the Americas and Europe. For travel information related to hepatitis E see: http://wwwnc.cdc.gov/travel/yellowbook/2010/chapter-5/hepatitis-e.aspx

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UPDATES